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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,868	08/11/2006	Roghieh Saffie	2491-66	4844

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EXAMINER	
WESTERBERG, NISSA M	

ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,868	SAFFIE ET AL.	
	Examiner	Art Unit	
	Nissa M. Westerberg	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/7/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 - 9, 13, 14, 18 - 21* is/are pending in the application.

4a) Of the above claim(s) *20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 - 9, 13, 14, 18, 19 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/21/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of group III, a method of treating cancer and an administration as in claim 21 of injecting a suspension of microparticles into the caner tumour in the reply filed on July 7, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

The search and examination have not been expanded beyond the elected species.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated

by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1 – 6 and 13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16 and 19 – 21 of copending Application No. 10/468742. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1 – 6 and 13 of the instant application are generic to all that is recited in claims 16 and 19 – 21 of '742. That is claims, 16 and 19 – 21 of '742 fall entirely within the scope of claims 1 – 6 and 13 or, in other words, claims 1 – 6 and 13 are anticipated by claims 16 and 19 – 21 of '742.

Specifically, the claims of the instant application recite a method of treating cancer by the administration of pharmaceutical composition comprising a cytotoxic drug and a porous carrier material, such as doped or undoped silicon. The claims of '742 recite a method of treating cancer by the administration a product comprising porous or polycrystalline silicone which has been doped with phosphorus that is transmuted to ^{32}P, a cytotoxic drug, that has been implanted into the tumor.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 6, 8, 9, 13, 14, 18 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Nsereko et al. (Biomaterials 2002).

Nsereko et al. discloses a preparation of biodegradable polymeric microparticles containing paclitaxel (p 2724, col 1, ¶ 3). The microparticles comprise chitin or chitin-PLURONIC® F-108 microparticles, a porous material. 100 mg of microparticles are impregnated with 1 mg of paclitaxel and dried (p 2725, section 2.5). The microparticles were suspended in a polyethylene glycol and administered subcutaneously at the base

of the tumor in a mouse (p 2726, section 2.6.3). This allows for the localized delivery of the potent anti-tumor agent paclitaxel (p 2730, section 4). Therefore, Nsereko et al. discloses the administration of a porous material and the cytotoxic drug paclitaxel directly into a tumor as a method of treating cancer.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1 – 4, 6, 8, 9, 13, 14, 18, 19 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Canham et al. (WO 02/067998) in view of Nsereko et al. (Biomaterials 2002).

Canham et al. discloses a product comprising an anticancer ingredient such as a radionuclide and/or at least one cytotoxic drug and a silicon component such as amorphous or resorbable silicon (p 3, ln 1 – 9). The microparticles can comprise at least part of the silicon component and at least part of the anticancer component and the product can comprise a multiplicity of silicon implants (p 4, ln 15 – 19). When used for the treatment of liver cancer, the product is delivered by injecting a suspension of microparticles into the hepatic artery (p 4, ln 28 – 30). When porous silicon is used as the silicon component, the cytotoxic drug is disposed in the pores (p 7, ln 11 – 14). The silicon can be resorbable to localize drug release at the site of the implant while allowing for the possibility of future implantation and/or diagnostic imaging of the patient (p 7, ln 16 – 23). Examples of cytotoxic drugs which may be used in the composition are given (p 8, ln 25 – 29).

Canham et al. does not explicitly teach injection of the suspension into the tumor or the inclusion of paclitaxel as the cytotoxic agent.

Nsereko et al. discloses a preparation of biodegradable polymeric microparticles containing paclitaxel (p 2724, col 1, ¶3). Paclitaxel would be a prime candidate for localized delivery to provide an excellent pharmacokinetic profile and therapeutic benefits (p 2723, col 2, ¶2). The microparticles were suspended in a polyethylene glycol and administered subcutaneously at the base of the tumor in a mouse (p 2726, section 2.6.3). This allows for the localized delivery of the potent anti-tumor agent paclitaxel (p 2730, section 4).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare the silicon microparticle containing cytotoxic agents as taught by Canham et al., and to use paclitaxel as the cytotoxic agent, taught by Nsereko et al. as a potent anti-cancer agent suited for localized delivery by release from porous microparticles. It also would have been obvious to inject the suspension directly into the tumor, and not simply into an artery in the organ with the tumor, as taught by Nsereko et al. Neither reference discloses the dose delivered of the cytotoxic drug and whether or not that dosage is higher than the LD50 of the cytotoxic drug in corresponding free form. The is no evidence to show that dosage delivered from the silicon microparticles as taught by Canham et al. would not be higher than that LD50 of the free cytotoxic drug. It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to

"prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

10. Claims 1 – 6, 8, 9, 13, 14, 18, 19 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Canham et al. and Nsereko et al. as applied to claims 1 – 4, 6, 8, 9, 13, 14, 18, 19 and 21 above, and further in view of Canham (US 6,322,895).

Canham et al. and Nsereko et al. disclose the treatment of cancer by the administration directly to the tumor of porous silicon microparticles containing a cytotoxic drug such as paclitaxel.

Neither reference discloses the use of mesoporous silicon as the carrier material. Mesoporous silicon has an average pore size of between 2 and 50 nm (¶ [0029] of the PGPub of the instant application). The pore size of the silicon used in Canham et al. is not disclosed.

US'895 discloses that mesoporous silicon wafers has a higher dissolution rate than microporous silicon and shows resorbable biomaterial characteristics (col 8, ln 17 – 23).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare a porous silicon microparticle preparation comprising paclitaxel as disclosed by Canham et al. and Nsereko et al. and to use mesoporous silicon as the porous carrier material, to provide a resorbable material with a higher dissolution rate, as taught by US'895.

11. Claims 1 – 4, 6 – 9, 13, 14, 18, 19 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Canham et al. and in view of Straub et al. (US 6,610,317).

Canham et al. discloses a product comprising an anticancer ingredient such as a radionuclide and/or at least one cytotoxic drug and a silicon component such as amorphous or resorbable silicon (p 3, ln 1 – 9). The microparticles can comprise at least part of the silicon component and at least part of the anticancer component and the product can comprise a multiplicity of silicon implants (p 4, ln 15 – 19). When used for the treatment of liver cancer, the product is delivered by injecting a suspension of microparticles into the hepatic artery (p 4, ln 28 – 30). When porous silicon is used as the silicon component, the cytotoxic drug is disposed in the pores (p 7, ln 11 – 14). The silicon can be resorbable to localize drug release at the site of the implant while allowing for the possibility of future implantation and/or diagnostic imaging of the patient (p 7, ln 16 – 23). Examples of cytotoxic drugs which may be used in the composition are given (p 8, ln 25 – 29).

Canham et al. does not explicitly teach injection of the suspension into the tumor, the inclusion of paclitaxel as the cytotoxic agent or the amount by weight of the cytotoxic agent present in the microparticles.

Straub discloses paclitaxel provided in a porous matrix form (col 1, ln 64 – 66). Paclitaxel has tremendous therapeutic potential but suffers from disadvantages such as poor aqueous solubility and precipitation in the blood (col 1, ln 14 – 37). The formulations can be administrated as a bolus in a reduced volume while avoiding precipitation and toxicity and can be administered by a number of routes, including

directly into the tumor (col 2, ln 34 – 41). The porous paclitaxel matrix most preferably contains between about 10% and about 70% by weight of paclitaxel, but the range can be a wide as 1% to 95% by weight (col 3, ln 9 – 11).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare porous silicon carriers comprising a cytotoxic agent as taught by Canham et al. and to use paclitaxel as the cytotoxic ingredient, which results in improved deliver of this potent cytotoxic agent, as taught by Straub et al. Straub et al. also discloses that this suspension can be directly administered to the tumor.

Neither reference discloses the dose delivered of the cytotoxic drug and whether or not that dosage is higher than the LD50 of the cytotoxic drug in corresponding free form. The is no evidence to show that dosage delivered from the silicon microparticles as taught by Canham et al. would not be higher than that LD50 of the free cytotoxic drug. It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

12. Claims 1 – 9, 13, 14, 18, 19 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Canham et al. and Straub et al. as applied to claims 1 – 4, 6 – 9, 13, 14, 18, 19 and 21 above, and further in view of Canham (US 6,322,895).

Canham et al. and Straub et al. disclose the treatment of cancer by the administration directly to the tumor of porous silicon microparticles containing a cytotoxic drug such as paclitaxel, which can contain significant amounts (up to 95% by weight) of the cytotoxic drug.

Neither reference discloses the use of mesoporous silicon as the carrier material. Mesoporous silicon has an average pore size of between 2 and 50 nm (¶ [0029] of the PGPub of the instant application). The pore size of the silicon used in Canham et al. is not disclosed.

US'895 discloses that mesoporous silicon wafers has a higher dissolution rate than microporous silicon and shows resorbable biomaterial characteristics (col 8, ln 17 – 23).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare a porous silicon microparticle preparation comprising paclitaxel as disclosed by Canham et al. and Straub et al. and to use mesoporous silicon as the porous carrier material, to provide a resorbable material with a higher dissolution rate, as taught by US'895.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8 a.m. - 4 p.m. ET. If

attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

NMW